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Parent-mediated interventions to promote communication and language development in children with Down syndrome aged between birth and six years

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To systematically assess the evidence for parent-mediated interventions aimed at improving communication and language development in children with Down syndrome aged between birth and six years.

As a secondary aim, we will examine the effects of the treatment on parental behaviour and responsivity. We will also assess the effects of the treatment on the children's non-verbal means of communicating and socialisation.

BACKGROUND

Description of the condition

Down syndrome is the most common genetic cause of intellectual disability and is due to extra genetic material on chromosome 21. The condition can be identified through prenatal screening and testing, or shortly after birth through clinical observations that are confirmed through genetic testing. The World Health Organization (WHO) estimates the incidence of Down syndrome to be between 1 in 1000 and 1 in 1100 live births worldwide. Rising maternal age over recent years has led to an increase in the

syndrome, although this is somewhat offset by prenatal screening and terminations, leading to wide variations in incidence across countries (Loane 2013). For example, Ireland had an incidence of approximately 23 per 10,000 of live births between 1990 and 2009, which was much higher than other European countries, including the United Kingdom (10 per 10,000), France (7 per 10,000) and Germany (8 per 10,000) (Loane 2013), and twice as high as that reported in the United States (11.8 per 10,000; Shin 2009). Shin 2009 also reported a higher incidence in Hispanic individuals compared to non-Hispanic white and African Americans. Three types of chromosomal anomalies lead to Down syndrome. The most common is trisomy 21 (present in 95% of

cases), followed by translocation (4%) and mosaicism (1%), the latter having better outcomes for language and cognitive abilities (Roizen 2007). Down syndrome is associated with a number of medical, physical and developmental difficulties, including motor and intellectual difficulties, although language is considered to be the area that is most impaired with the greatest effect on independent living (Abbeduto 2007).

The intellect of children with Down syndrome varies widely, although most fall in the moderate range of intellectual disability (Roizen 2007). A meta-analysis of speech and language skills in children with Down syndrome found similar variability, although most had an impairment when compared to typically developing children of the same non-verbal mental age (Næss 2011). One exception was vocabulary comprehension, which was in line with the children's non-verbal mental age. Young children with Down syndrome are often reported to progress through stages and sequences of language and early communication development similar to those of younger, typically developing children (Chapman 1997), albeit at a slower pace. This progress leads to an overall profile of delayed early language development (Polišenská 2014), although differences have also been described (Ypsilanti 2008). The general profile of language difficulties in children with Down syndrome is poorer expressive language when compared to language comprehension, particularly in the area of vocabulary, although for grammar, both receptive and expressive difficulties have been found (Laws 2004; Miller 1999). The heterogeneity of language development in this population has been well documented, and although most children are delayed in the onset of their first words (Roizen 2007), others have found that some children start using words at a similar age to typically developing children (Chapman 1997). However, the gap in language attainment between children with Down syndrome and their typically developing peers, even those of the same non-verbal mental age, tends to widen with increasing age. Some studies have reported a plateau in linguistic attainment in adolescents, particularly for expressive language, morphosyntax (Laws 2004), and narrative production (Chapman 1998), although others have shown that they can continue to make gains in their language development into adulthood (Abbeduto 2007; Chapman 2001). More importantly, the language abilities of children with Down syndrome have been found to be even more delayed than would be expected from their overall level of cognitive functioning, indicating a form of specific speech and language impairment relative to their non-verbal mental age (Buckley 2002; Laws 2003; Niccols 2002; Vicari 2000). Furthermore, these children have been found to perform more poorly on measures of speech and language development than mental-aged-matched peers with other cognitive difficulties (Roberts 2008). A significant contributor to speech and language impairment in this population is the high rate of hearing loss (Laws 2014), particularly fluctuating conductive hearing loss from frequent middle ear infections, which has been observed to affect 93% of one-year olds, with 68% still affected at five years (Barr 2011). Deficits in auditory (phono-

logical), short-term memory have also been linked to language difficulties in this population (Chapman 2001; Laws 2003), as have early difficulties with joint attention (Zampini 2015). Their language difficulties are compounded by deficits in speech sound production and intelligibility (Kent 2013). Areas of relative strength for children with Down syndrome are in socialisation and non-verbal communication through the use of gestures (Chapman 1997). Moreover, they can have a preference for gestures over verbal communication early in development, and a positive relationship between gesture use and later expressive language has been found (Te Kaat-van den Os 2015).

Description of the intervention

Unlike other groups of children with speech and language delay, children with Down syndrome are identified at birth and so intervention begins in infancy, involving parents and caregivers. Training parents to be their child's main therapist is important as research has identified that the ways in which parents interact with their children influences their cognitive and communication development. Furthermore, parent-child interaction has been observed to be disrupted by the presence of Down syndrome as early as five months of age (Slonims 2006). One important aspect of parent-child interaction is responsiveness. For example, Mahoney 1985 found that children with Down syndrome had higher scores on the mental domain of the Bayley Scales of Infant Development (BSID) if their mothers used a more responsive interaction style when playing with them (Bayley 1969), compared to children who had mothers that used a more directive or teaching style of interaction. A follow-up study demonstrated that maternal responsiveness was associated with increased use of words, imitation, and non-verbal communication in the children when compared to those with mothers who used a didactic or inattentive style of interaction (Mahoney 1988). Caregivers can also influence their child's language development through the quality and quantity of their linguistic input. For example, Huttenlocher 2010 identified that the diversity of language input received by children predicts their language growth, although the language learning environment is heavily influenced by parental socioeconomic status (Hart 1995; Hoff 2006). For young children with Down syndrome, research has identified that the vocabulary directed to them can be simpler, in terms of composition and variability, when compared to typically developing peers (Zampini 2011). This study also showed that the children with Down syndrome received lower proportions of imitations from their mothers than their peers, which has implications for their language learning experiences.

Therefore, a large part of speech and language intervention for young children with Down syndrome involves training parents and caregivers about the importance of the quality and quantity of their language input and interaction to maximise cognitive, social and communication development. The most frequent intervention is through a model known variously as '(interactive) fo-

cused stimulation', 'responsivity education/teaching' or 'naturalistic teaching'. The aim of this intervention is to train caregivers to recognise and respond to non-verbal communication and socialisation in their children in order to encourage an increase in these behaviours and a move towards more conventional (verbal) means of communicating (Warren 2008). One example is the Hanen programme for parents 'It Takes Two to Talk' (Girolametto 2006), which educates parents about the importance of child-oriented behaviours to promote joint attention and reciprocal interaction and helps them to apply language facilitation strategies in natural, everyday interactions. Enhanced Milieu Teaching (EMT) is another version of this intervention, which combines elements of responsivity education with behavioural strategies and milieu teaching through modelling and appropriate environmental arrangements (Hancock 2007). Some programmes (such as prelinguistic milieu teaching) combine elements of parent-mediated intervention with direct clinician intervention, but the focus of this review will be on the effects of parent-mediated interventions to determine the impact on children's language and communication development. Although other programmes may encourage parents to explicitly teach their children manual signs or key-word reading, this review will focus on interventions that target interactive learning through daily activities and play.

Parent-mediated interventions often take place in group classroom sessions where caregivers learn about communication strategies and are then regularly videotaped interacting with their child by the clinician in order to provide feedback and reinforcement of goals for that individual parent-child dyad (Girolametto 2006). Alternatively, the intervention can be delivered on an individual basis, where a clinician and parent work together to devise goals for both the parent and child, and the parent is coached by the clinician through discussion, role-play, and video-feedback on how to implement strategies to achieve these goals. Therefore, the outcomes of the intervention are measured primarily in terms of changes in the child's interaction, communication and language skills but also through changes in caregiver behaviour and responsivity, as this is a key factor in the success of the programmes.

As language is acquired in everyday interactions between children and their caregivers, and as parents and caregivers spend the most time interacting and communicating with their children, this intervention is considered to be ecologically valid and family-centred. Furthermore, best practice guidelines for speech and language therapy with preschool children with Down syndrome highlight the importance of parents being aware of, and trained in, effective strategies for promoting language and communication as they are their child's best therapist, and that this intervention should take place as early as possible (Buckley 2002). Overall, Roizen 2007 maintains that speech and language therapy addressing expressive language and intelligibility is needed for many years with this population.

How the intervention might work

Parent-mediated interventions come from naturalistic observations of the bi-directional nature of adult-child interactions, whereby an increase in non-verbal or verbal communication from the child changes how the adult responds (known as contingent responses), which in turn helps to support further communication development in the child (Warren 2008). This means that both the child and those in their communicative environment change over time and affect each other in a reciprocal fashion. However, the interventions presume that as children with language delay have difficulty picking up on parental cues, or that as both caregivers and children interact and respond differently when compared to typically developing children, more tailored, focused and intensive caregiver input is required. The interventions are thought to work by helping adults to become aware of the children's communication and interaction and changing their responses to their children. This aims to help children increase their frequency of intentional communication through joint attention and verbal or non-verbal communication, or both (for example, pointing and gestures), thereby preparing children to use early language skills more efficiently (Warren 2008). Other versions of the intervention, such as EMT, take a hybrid approach by including principles from operant conditioning to reinforce children's communicative responses to adult prompts and teach targeted vocabulary and grammar goals for the child (Hancock 2007). The more structured approaches aim to make caregivers aware of the quality and quantity of their linguistic input to the children, and modify it according to the ability of the child, which helps them to understand and eventually use language themselves (Girolametto 1996). The aims of parent-mediated interventions are therefore as follows:

1. To foster and increase adult-child interaction and joint attention through child-centred activities;
 2. To promote the frequency and complexity of adult responsivity to non-verbal and verbal communication; and
 3. To facilitate appropriate language modelling and input from adults that helps the child to understand and produce language.
- The model of parent-mediated interventions is 'triadic' (Roberts 2011), with an experienced clinician training parents to use specific interaction- and language-promoting strategies with their children. This means that there are many aspects that can influence the overall effectiveness of the intervention, including how the intervention is delivered and by whom, parental implementation of the strategies and the child's ability to benefit from the same. For example, a previous study noted that maternal style of interaction and level of education before treatment affected the outcome of a similar intervention (Yodor 1998). Other factors that might influence the outcome include the caregiver's relationship with the clinician, their willingness to implement the intervention and their learning styles. How the intervention is delivered (for example, group or individually), the intensity of delivery as well as the training and experience of the clinician delivering the inter-

vention may also have an effect. For the children, previous research has noted that baseline language and cognitive skills can influence a child's response to this type of intervention (Siller 2013); and similarly, the child's general health, hearing status, personality and behaviour could be important mediators of treatment gains. We will attempt to extract this information from the studies, where provided, in order to understand these complex factors that make this intervention work.

Why it is important to do this review

Experts in the field of Down syndrome argue that “speech and language therapy is the most important part of intervention services for children with Down syndrome if we wish to promote their cognitive ... and social development” (Buckley 2002, p 70). To date, however, there has been no systematic review of any speech and language intervention for children with Down syndrome. Changes in healthcare services for young children have moved towards providing for the needs of the whole family through initiatives such as Individualised Family Service Plans (IFSPs), which outline the support required by the whole family. As parents are best placed to facilitate their child's main language, largely because they are able to maximise communication opportunities in everyday situations (Girolametto 2006), early intervention services are now embedded in the home and mediated through parents and caregivers (Kaiser 2011). The aim of this early intervention is to enhance family patterns of interaction within a transactional model of development that can change the child's actual and potential outcomes at an early and malleable stage of development. Sameroff 2000 (p 142) says that a child's development is “... a product of the continuous dynamic interactions between the child and the experience provided by his or her family and social context”. Thus, interventions that enhance those interactions with very young children are appropriate and well placed to support the most positive outcomes. However, the evidence base for these interventions has not yet been established for this group. Furthermore, the various parent, child and therapy factors that influence the success of the intervention are not yet known. Roberts 2011 carried out a meta-analysis into the effectiveness of parent-implemented language interventions but this review was not limited to randomised controlled trials (RCTs) and children with any type of language impairment were included. Cochrane systematic reviews on speech and language interventions exist for other identifiable groups of children with language difficulties such as children with cerebral palsy (Pennington 2003) and primary speech and language delay or disorder (Law 2003), although both of these reviews are significantly out of date. In addition, there are systematic reviews of parent-mediated interventions for children with autism spectrum disorders (Oono 2013) and attention deficit hyperactivity disorder (ADHD; Zwi 2011), but as yet, there are no reviews of parent-mediated interventions for this population. Finally, as parent-mediated interventions are considered to be ‘indirect’, parents may

be resistant of an intervention that removes direct clinician-child contact or become more stressed by having to be directly responsible for their children's intervention when they are already dealing with the additional demands of having a child with a disability (Brinker 1994). If early parent-mediated interventions are to continue, we need to gather the evidence for the effects on the child's language and other communication skills, and the specific factors that are likely to make them more successful. It is anticipated that the findings from this review will help inform clinicians, parents, and educators about best practice in early intervention for children with Down syndrome.

OBJECTIVES

To systematically assess the evidence for parent-mediated interventions aimed at improving communication and language development in children with Down syndrome aged between birth and six years.

As a secondary aim, we will examine the effects of the treatment on parental behaviour and responsivity. We will also assess the effects of the treatment on the children's non-verbal means of communicating and socialisation.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and quasi-RCTs (studies where participants are allocated to treatments by, for example, date of birth, location or alternate allocation) of parent-mediated interventions targeting language skills for children with Down syndrome. We will not include cross-over designs as these are not considered appropriate for interventions with lasting consequences.

Types of participants

Primary caregivers of children with Down syndrome aged between birth and six years, irrespective of severity or type. All children must be monolingual but can speak any language.

The term ‘caregiver’ includes grandparents and other caregivers who take on the ‘parent’ role for the purposes of the intervention. Studies that include children with Down syndrome as part of a group of children with intellectual disabilities will be included if separate results are available for the group with Down syndrome.

Types of interventions

All parent-mediated interventions designed to improve communication and language in children with Down syndrome from birth to six years of age. The intervention will involve coaching, supervision and support from a clinician and will take place either on an individual or group basis. Specifically, we will make comparisons between the parent-mediated interventions and the following:

1. General stimulation conditions or 'teaching/therapy as usual (TAU)';
2. Interventions that use clinician-mediated interventions; and
3. Controlled conditions that involve no treatment or delayed (wait-listed) treatment.

We will include studies in which the parent-mediated intervention is delivered in conjunction with another intervention, such as a clinician-mediated intervention, as long as the latter is given to both experimental and control groups, and the parent-mediated intervention is provided only to those in the experimental group.

Types of outcome measures

Primary outcomes

Expressive and receptive language skills as measured through scores from standardised tests, criterion referenced tests, parent reports, experimental tasks, and language samples/conversations (for example, The Reynell Developmental Language Scales (RDLS), [Edwards 1997](#)). We will use standardised scores where provided, or raw scores derived from standardised tests, or both. The scores from language samples will include mean length of utterance (MLU) as measured in words or morphemes, number of different words (NDW) in a sample, or total number of words (TNW) and can be used to calculate type-token ratios (TTRs).

We will consider both the level of language development as well as rate of development (as indicated by the change in scores) although we will analyse these separately. Furthermore, we will measure the effects of the interventions at the following time points:

1. Immediately: within one month after the end of the intervention;
2. Short to medium term: one to 12 months after the end of the intervention; and
3. Long term: one to two years after the end of an intervention.

We will also measure possible adverse effects of intervention such as an increase in parental stress (as measured by, for example, the Parenting Stress Index (PSI); [Abidin 1995](#)).

Secondary outcomes

Secondary outcomes include changes in parental behaviours/responsivity captured through video-taped interactions or observations and measured by a validated scale (for example, the Maternal Behaviour Rating Scale (MBRS; [Mahoney 1999](#)), as well

as parental satisfaction with the intervention as measured by questionnaires and interviews. We will also measure child-related changes in non-verbal communication (for example, pointing/gestures, use of signs) and socialisation (for example, requesting/commenting) as assessed through naturalistic observations or video-taped interactions and validated checklists such as the MacArthur-Bates Communicative Development Inventories (CDIs; [Fenson 2007](#)).

We will consider possible secondary adverse effects of the intervention such as an increase in negative behaviour in the child (as measured by the Maladaptive Behaviour Index (MBI) subscale of the Vineland Adaptive Behavior Scales (VABS; [Sparrow 2005](#)) or other validated scales) or language attrition (as indicated by a reduction in scores from baseline language tests). We will also measure the compliance with treatment, such as any non-attendance or non-completion of home practice by the parents as measured and reported by the authors in the study, and any reasons for the same.

All of the primary and secondary outcomes will be used to populate the 'Summary of findings' table.

Search methods for identification of studies

Electronic searches

We will search the following databases and trial registers to identify relevant trials:

1. Cochrane Central Register of Controlled Trials (CENTRAL, current issue, part of *The Cochrane Library*), and which includes the specialised register of the Cochrane Developmental, Psychosocial and Learning Problems Group;
2. Ovid MEDLINE (1946 to current);
3. Embase (1980 to current, Ovid);
4. ERIC (1966 to current, ProQuest);
5. PsycINFO (1806 to current, Ovid);
6. CINAHL Plus (1937 to current, EBSCOhost);
7. Social Citation Index (SCI, 1970 to current, Web of Science);
8. Social Sciences Citation Index (SSCI, 1970 to current, Web of Science);
9. Cochrane Database of Systematic Reviews (CDSR, current issue, part of *The Cochrane Library*);
10. Database of Abstracts of Reviews of Effects (DARE, current issue, part of *The Cochrane Library*);
11. Academic Search Complete (all available years, EBSCOhost);
12. ProQuest Dissertations and Theses (UK & Ireland, 1990 to current);
13. ProQuest Dissertations and Theses (A&I, 1970 to current);
14. LILACS (all available years, lilacs.bvsalud.org/en/);
15. SpeechBITE (all available years, speechbite.com);

16. UKCRN Portfolio Database (all available years, public.ukcrn.org.uk/search/);
17. Clinical Trials.gov (all available years, clinicaltrials.gov); and
18. World Health Organization International Clinical Trials Registry Platform (WHO ICTRP, all available years, apps.who.int/trialsearch/default.aspx).

We will search Ovid MEDLINE using the search strategy in [Appendix 1](#) and modify it appropriately for other databases. We will not apply any restrictions on date, language or publication status. We will seek translations when necessary.

Searching other resources

We will handsearch the reference lists of relevant journal papers, book chapters, and systematic reviews identified by the electronic searches. We will approach relevant professional organisations, such as Down Syndrome Education International (dseinternational.org), search the website of The Hanen Centre (hanen.org), and email colleagues and researchers to identify other possible published and unpublished studies such as technical or research reports, conference abstracts and dissertations, or ongoing trials. We will also search 'WhatWorks' (thecommunicationtrust.org.uk/whatworks), an online resource, which summarises research on intervention for speech, language and communication, based on the Better Communication Research Programme in the UK.

Data collection and analysis

Selection of studies

We will pilot interpretation and implementation of the eligibility criteria for including/excluding studies on a sample of reports prior to selecting the final studies. We will then refine and clarify the eligibility criteria and ensure that there is agreement among those authors who will be selecting the studies. One review author (COT) will then conduct the literature search. We will manage all references generated from the search strategy using a reference management programme ([EndNote X7](#)); any duplicate records of the same report will be removed. The two first authors (COT and AS-YL) will independently conduct an initial screening of titles and abstracts to eliminate any references that are obviously irrelevant to the review and identify relevant studies based on our inclusion/exclusion criteria. In cases where an abstract contains insufficient information for judging whether a study meets the inclusion criteria, we will retrieve the full text to independently examine compliance with our eligibility criteria. We will link together multiple reports of the same study. In the event of disagreement over the inclusion/exclusion of a particular paper, a third author (FEG) will be consulted for arbitration. We will report the disagreement, including the title(s) and reason(s) for the different judgements

between the two review authors, and the consensus obtained after discussion. We will complete a PRISMA flowchart to describe the study selection process before moving to data collection and extraction.

Data extraction and management

We will develop and pilot a data extraction form based on the inclusion/exclusion criteria (for example, only RCTs or quasi-RCTs will be included, no single case studies). COT and AS-YL will independently extract the following information from each paper.

1. Participants: number; age (of caregivers and children); gender (of caregivers and children); caregiver status (parent/other); inclusion and exclusion criteria; child intelligence quotient (IQ); socioeconomic status (for example, maternal education/income); hearing status; health status (of caregivers and children); comorbid conditions (for example, autism); and attendance at preschool or other therapy/educational settings.
 2. Methods: baseline language and communication assessment(s); outcome measure(s) used and assessment results (for example, number of words said or understood); secondary outcomes, including any measures of caregiver behaviour/responsivity or stress through validated scales; and child measures of changes in non-verbal communication and socialisation. We will also record the timing of the outcome measurement.
 3. Interventions: number of intervention sessions given; mode of delivery (for example, group/individual; clinic/classroom based; and whether video feedback was used); frequency and number of the intervention sessions; duration of the intervention sessions; date and location; qualifications and experience of clinician; and whether adherence was evaluated.
 4. Intervention integrity: we will record the presence or absence of features of fidelity verification, compliance, and promotion using the categories proposed by [Dane 1988](#). Any sources of funding for the study will also be recorded.
- All extracted data will be entered into Review Manager 5 software ([RevMan 2014](#)) by the first author (COT) and will be checked for accuracy against the data extraction sheet by the second author (AS-YL), working independently.

Assessment of risk of bias in included studies

Two authors (COT and AS-YL), working independently, will rate the risk of bias in each included study using the Cochrane's tool for assessing risk of bias as described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). Final judgement of risk of bias will be reached by consensus. If agreement cannot be reached, a third author (FEG) will be consulted for arbitration. The assessment will consist of two parts: (1) a succinct description, which will include verbatim quotes from the study reports or correspondence with the trial author(s), or a comment from the review author about the procedures used to avoid bias,

or both; and (2) an assessment of the risk of bias by assigning a rating of the likely risk of bias for the adequacy of the following domains.

Sequence generation

We will outline the methods used to generate the allocation sequence in sufficient detail so as to assess whether it should have produced comparable groups, using quotes wherever possible. We will add a comment, such as 'probably done' or 'probably not done', to supplement any ambiguous quote. We will assign each included study to one of the following categories:

1. 'Low risk', which indicates an adequate method was used for randomisation (for example, coin toss or table of random numbers);
2. 'High risk', which indicates that an inadequate method of randomisation was used (for example, case file number, date of birth or alternate numbers); or
3. 'Unclear risk', which indicates uncertainty about whether an appropriate method of randomisation was used.

Allocation concealment

We will describe the methods used to conceal the allocation sequence in sufficient detail to determine whether intervention allocation could have been foreseen in advance of, or during, recruitment and assign the included studies to one of the following criteria:

1. 'Low risk', which indicates an adequate concealment of allocation (for example, pre-numbered or coded identical containers administered serially to participants);
2. 'High risk', which indicates that the allocation was not adequately concealed (for example, alternate assignment); or
3. 'Unclear risk', which indicates uncertainty about whether the allocation was adequately concealed (for example, the authors did not describe the allocation methods).

Blinding of participants and personnel

As this review is addressing parent-mediated interventions, it is not possible (or highly unlikely) that participants who receive the intervention (the caregivers) and the personnel who deliver the intervention (that is, the clinicians) will have been blinded to the type of intervention received. However, we will describe the methods used, if any, to blind study participants and personnel from knowledge of which intervention was received for each included study. We will assess the risk of bias that resulted from any lack of blinding on a case-by-case basis, using the categories listed below (though it is likely that the risk of bias for most of the included studies will be 'high'):

1. 'Low risk', which indicates that participants and personnel are blinded or we judge that the lack of blinding would be unlikely to affect results;

2. 'High risk', which indicates that some participants or key study personnel are not blinded, and the lack of blinding is likely to introduce bias; or blinding of key study participants and personnel was attempted, but it is likely that the blinding could have been broken; or

3. 'Unclear risk', which indicates that insufficient information was provided to permit a judgement of low or high risk of bias.

Blinding of outcome assessment

For each included study, we will describe the methods used, if any, to blind outcome assessor(s) from knowledge of which intervention a participant received. Assessment will be made for each main outcome (for example, outcome measures at six and 12 months post-therapy). We will grade this domain as:

1. 'Low risk', which indicates that blinding of participants and key study personnel was ensured, and it is unlikely that the blinding could have been broken;
2. 'High risk', which indicates no blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding; or
3. 'Unclear risk', which indicates that the study did not address this outcome.

Incomplete outcome data

We will describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. We will report the numbers in each intervention group (compared with total randomised participants), the reason(s) for attrition/exclusion where provided, and any re-inclusions in analyses performed by the review authors. We will grade this domain as:

1. 'Low risk', which indicates no missing outcome data; reasons for missing outcome data unlikely to be related to the true outcome; or missing outcome data balanced across groups;
2. 'High risk', which indicates that the reason for missing outcome data is likely to be related to the true outcome; or
3. 'Unclear risk', which indicates that insufficient information was provided to permit a judgement of low or high risk of bias.

Selective outcome reporting bias

We will assess the possibility of selective outcome reporting by the study authors by checking whether any of the stated outcomes were not reported at the end of the study. We will assess this by checking the trial protocol, if available from trial registry or from study authors. We will assign each included study to one of the following categories:

1. 'Low risk', which indicates that the studies have reported all pre-specified outcomes;
2. 'High risk', which indicates that selective reporting of outcomes is evident in the study; or

3. 'Unclear risk', which indicates uncertainty about whether a selective outcome reporting bias is avoided.

Other sources of bias

We will describe any additional problems that may put a study at risk of bias. We will grade this domain as:

1. 'Low risk', which indicates that the study is free from other sources of bias;
2. 'High risk', which indicates that there is at least one important risk of bias (for example, baseline imbalance, early stopping, and co-intervention such as participants receiving additional treatment outside of the study protocol of parent-mediated intervention); or
3. 'Unclear risk', which indicates that insufficient information was provided to permit a judgement of low or high risk of bias.

Measures of treatment effect

Binary and categorical data

Binary or dichotomous data (for example, vocabulary improvement versus no change) may occur. Categorical data may also be presented where ordinal measurement scales are used. We will analyse these data by calculating the odds ratio (OR) with a 95% confidence interval (CI).

Continuous data

Most data from the expected outcome measures are likely to be continuous data such as standardised language test results, mean length of utterance (in words or morphemes), number of different words, and total number of words as derived from spontaneous language samples. Similarly, secondary outcomes (for example, changes in parental and child interactional behaviours) are also likely to be continuous data. Where possible, we will extract the numbers of participants, means and standard deviations (SD) in the intervention and control groups. We will use change-from-baseline scores (change scores) and post-test only scores if the required means and SDs are available, as we expect to find only a small number of RCTs thus making comparability at baseline problematic. We will analyse change scores and post-test scores separately. However, if all studies measure outcomes using a uniform measurement scale, we will combine the different types of analyses using the (unstandardised) mean difference (MD or the 'difference in means') method in RevMan (Deeks 2011). Where studies measure the same outcome using different methods, we will use the standardised mean difference (SMD) to combine studies with the 95% CI as a summary statistic. We will use Hedges's g to calculate the effect size as it is more appropriate for studies with small samples as is expected in this review (Hedges 1985). Given the nature of child language assessment, it is likely that studies

will use different methods of administration (for example, parental questionnaires versus direct assessment) and measure different aspects of language (comprehension versus expression). Therefore, we may need to conduct separate analyses for these outcomes.

Unit of analysis issues

Cluster-randomised trials

It is possible that we will include cluster-randomised trials in this review (for example, groups of children attending different clinics or preschools). In this case, appropriate statistical approaches should be used; for example, using a two-sample t -test to compare the means of the cluster in the intervention group at cluster level, or a mixed-effects linear regression approach at individual level (Donner 2000). We will contact the trial author(s) if it is unclear that appropriate adjustments have been made (Donner 2000). If individual level data cannot be secured, we will control the data for the clustering effects using the procedures described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This will either be by extracting the number of clusters (or groups) randomised to each intervention group or the average (mean) size of each cluster; by extracting the outcome data ignoring the cluster design for the total number of individuals (for example, means and SDs); or by extracting an estimate of the intracluster correlation coefficient (ICC). We will obtain an appropriate ICC by using external estimates obtained from similar studies, and if this cannot be achieved we will explore the impact of the inclusion of data from cluster-randomised trials by imputing a set of ICCs (for example, high (0.1), moderate (0.01), and small (0.001) ICC). We will calculate the inflated standard errors that account for clustering by multiplying the standard errors of the effect estimate by the square root of the design effect as outlined in Higgins 2011 (Chapter 16.3.6). We will combine the results with those from individually randomised trials for meta-analysis using the generic inverse variance method in RevMan, providing that clinical heterogeneity between the studies is small (Donner 2000; Higgins 2011).

Multi-arm studies

For studies that compare more than two intervention groups, we intend to combine results across eligible intervention groups (that is, parent-mediated interventions) to form a single intervention group and use pair-wise comparisons to compare these with all eligible control groups combined to form a single control group. We will give detailed descriptions of the intervention groups and the nature of each study in the 'Notes' and 'Interventions' sections of the 'Characteristics of included studies' tables.

Dealing with missing data

We will contact the authors of the included studies, where necessary, and ask them to supply any missing data or relevant unreported information. We will describe the missing data and the reasons, numbers and characteristics of dropouts/attrition for each included study in the 'Risk of bias' tables beneath the 'Characteristics of included studies' tables. We will consult the *Cochrane Handbook for Systematic Reviews of Interventions* for options for dealing with missing data (Higgins 2011). If the data appear to be missing at random, we will analyse the available data only. If data are not missing at random, we will impute the missing data with replacement values and treat these as if they were observed. For missing continuous data, we will impute the missing data either by using last observation carried forward (LOCF) or mean scores. For dichotomous data, we will perform a sensitivity analysis based on 'best' and 'worst' case scenarios to assess how results are sensitive to changes in the missing data (Gamble 2005). A best case scenario is where all participants with missing outcomes in the intervention group had good outcomes, and those in the control group had poor outcomes; a worst case scenario is the reverse. We will address the potential impact of missing data on the findings of the review in the Discussion section.

Assessment of heterogeneity

We will assess clinical heterogeneity by considering the variability in the participants (for example, socioeconomic status, age of parents and children, health status and linguistic abilities of the children), trial factors (for example, duration and intensity of the interventions, randomised concealment), and outcomes (for example, parent report versus direct assessment) studied. Should we identify any unexpected variability in these areas we will discuss it in full. We will assess statistical heterogeneity by using the Chi² test for heterogeneity, through visual inspection of forest plots, and by using the I² statistic (Higgins 2002; Higgins 2003). As the Chi² test has low power in a meta-analysis of a small sample of studies, we will use the recommended P value of 0.10 (rather than the typical value of 0.05) to determine statistical significance (Deeks 2011). In addition to a test of statistical heterogeneity, we will use the I² statistic to detect inconsistencies across studies. We will use the formula and guidelines for interpreting the outcomes outlined in Deeks 2011 (section 9.5.2), which includes taking the magnitude and direction of effects into account as well as the strength of evidence for statistical heterogeneity (for example, a CI for I²).

Assessment of reporting biases

Funnel plots (estimated differences in intervention effect sizes against their standard error) will be drawn if we find sufficient studies (N = 10). An asymmetric appearance of the funnel plot might indicate a relationship between effect size and study size, which would suggest the possibility of either reporting bias or poor

methodological quality in small studies leading to inflated effects. If funnel plot asymmetry is identified, and there are at least 10 studies included in the meta-analysis, we will consult a statistician for assistance in implementing statistical tests for funnel plot asymmetry in line with recommendations in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Should a relationship between trial and effect size emerge, we will examine the clinical diversity of the studies (for example, sample size or use of blinded outcome measures).

Data synthesis

We will carry out meta-analysis using Review Manager 5 (RevMan 2014), if there are sufficient data and where the interventions are similar in terms of the characteristics of the participants, the ways in which parent-mediated interventions are delivered, the frequency and duration of interventions, and the outcome measures used. We will apply both fixed-effect and random-effects models and compare the results to assess the impact of statistical heterogeneity. We will present the results from the random-effects model only, unless contraindicated (for example, if there are large differences between the results from fixed-effect and random-effects meta-analyses or if there is funnel plot asymmetry). In the case of serious funnel plot asymmetry, we will present both fixed-effect and random-effects analyses, under the assumption that asymmetry suggests that neither model is appropriate. If the same outcome is presented as dichotomous data in some studies and as continuous data in other studies, we will convert odds ratios (OR) for the dichotomous data to standardised mean differences (SMD) if it can be assumed that the underlying continuous measurements follow a normal or logistic distribution. Otherwise, we will conduct separate analyses.

Quality of evidence

We will assess the overall quality of the body of evidence using the 'GRADE' (Grades of Recommendations, Assessment, Development and Evaluation) approach (GRADE 2008). The GRADE Working Group outline five factors that may decrease the quality of a body of evidence. These are: limitations in the design and implementation of available studies (high likelihood of bias), inconsistency (unexplained heterogeneity), indirectness (population, intervention, comparison, and outcome), imprecision of results, or high probability of publication bias. We will assess the quality of the body of evidence against these criteria and assign it a judgement of 'high', 'moderate', 'low', or 'very low' quality. This information will be reported in the 'Summary of findings' table, which will be constructed using GRADE profiler (GRADEproGDT 2015).

Subgroup analysis and investigation of heterogeneity

If we identify sufficiently homogenous studies, we will conduct subgroup analyses to assess the impact of the following:

1. The age of the children (for example, birth to three years versus three to six years);
2. Mode of delivery (for example, group versus individual treatment);
3. Duration and intensity of therapy (determined by the length and frequency of the intervention respectively); and
4. Socioeconomic status of the family (for example, as measured through maternal education).

Sensitivity analysis

We will conduct a sensitivity analysis to examine the impact of study quality on the robustness of the conclusions drawn. This will be based on our assessment of the risk of bias concerning the quality of factors such as randomisation, blinding to outcome assessment,

and completeness of data. We will include in the analysis studies that we categorised as low or unclear risk of bias for these factors.

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* Indicates the major publication for the study

APPENDICES

Appendix I. Ovid MEDLINE search strategy

- 1 Down Syndrome/
- 2 (down\$ adj syndrome).tw.
- 3 Downs disease.tw.
- 4 trisomy 21.tw.
- 5 chromosome 21.tw.
- 6 (mongol or mongols or mongoloid or mongolism).tw.
- 7 Intellectual Disability/
- 8 Developmental disabilities/
- 9 ((intellectual\$ or learning) adj3 (disabilit\$ or disabl\$)).tw.
- 10 (developmental\$ adj3 (delay\$ or disabilit\$ or disabl\$)).tw.
- 11 mental\$ retard\$.tw.
- 12 or/1-11
- 13 exp child/
- 14 (child* or infant* or babies or baby or toddler* or girl* or boy* or pre-school* or preschool* or nurser* or kindergarten* or kindergarten*).tw.
- 15 or/13-14
- 16 12 and 15
- 17 exp Parent-Child Relations/
- 18 Parenting/
- 19 exp Parents/
- 20 Caregivers/
- 21 or/17-20
- 22 education/
- 23 teaching/
- 24 “Early intervention (Education)”/
- 25 early intervent\$.tw.
- 26 Education of Intellectually Disabled/

27 education, special/
 28 language therapy/
 29 speech therapy/
 30 (speech\$ or languag\$ or communicat\$ or sign\$ or nonverbal\$ or non-verbal\$ or cue\$).tw.
 31 Sign language/
 32 Manual Communication/
 33 Nonverbal communication/
 34 or/22-33
 35 21 and 34
 36 exp Parents/ed [Education]
 37 Caregivers/ed [Education]
 38 ((parent\$ or maternal\$ or mother\$ or father\$ or paternal\$ or carer\$ or caregiver\$ or care-giver\$) adj3 (coach\$ or educat\$ or intervention\$ or learn\$ or program\$ or teach\$ or train\$)).tw.
 39 ((parent\$ or maternal\$ or mother\$ or father\$ or paternal\$ or carer\$ or caregiver\$ or care-giver\$) adj3 (interact\$ or inter-act\$ or involv\$ or mediat\$ or respon\$)).tw.
 40 or/36-39
 41 focus?ed stimulation.tw.
 42 (naturalistic adj2 teaching).tw.
 43 (milieu adj2 teaching).tw.
 44 (responsiv\$ adj2 education).tw.
 45 (responsiv\$ adj2 teaching).tw.
 46 Hanen\$.tw.
 47 or/41-46
 48 35 or 40 or 47
 49 16 and 48
 50 randomized controlled trial.pt.
 51 controlled clinical trial.pt.
 52 randomi#ed.ab.
 53 placebo\$.ab.
 54 drug therapy.fs.
 55 randomly.ab.
 56 trial.ab.
 57 groups.ab.
 58 or/50-57
 59 exp animals/ not humans.sh.
 60 58 not 59
 61 49 and 60

CONTRIBUTIONS OF AUTHORS

COT, AS-YL, and FEG planned the review. COT wrote the protocol and developed the search strategy, with advice from AS-YL, FEG, AKvB, and PC. NJH provided feedback on the accessibility of the information to services users. COT has overall responsibility for the review.

DECLARATIONS OF INTEREST

Ciara O'Toole - received a Health Research Board Cochrane Fellowship Grant to assist in completing this work. The fellowship was received in January 2015, lasts for two years and pays for teaching cover and training support. Ciara's institution received a grant from Foras Na Gaeilge for a project looking at early language acquisition of Irish.

Alice S-Y Lee - none known.

Fiona E Gibbon - was paid an honorarium from the University of Hong Kong for advice on a research strategy for Research Assessment Exercise and paid a fee from Newcastle University for being an external participant on Internal Subject Review. Her institution receives funding from the Health Research Board. FEG receives royalties as Co-Editor of the Handbook of Clinical Phonetics. FEG has shares in various companies, which she confirms do not have a real or potential vested interest in the findings of the review.

Anne K van Bysterveldt - received fees from the Christchurch District Health Board for the supervision of a staff member. AKvB's current position at the University of Canterbury involves the development and delivery of postgraduate courses in the field of special education, for professionals working with children with disabilities and their families. She also provides clinical supervision in a similar field and has recently examined a thesis in the early intervention context. AKvB receives fees from the University of Melbourne for PhD thesis examination.

Paul Conway - none known.

Nicola J Hart - is a speech and language therapist and works for a charity, which advocates for people with Down syndrome and their families.

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- No sources of support supplied

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